REMARKS

The application has been amended to place the application in condition for allowance at the time of the next Official Action.

Claims 1-7 are pending in the application. Claim 1 is amended herewith.

Applicants note with appreciation the indication that claims 4 and 7 are allowed.

The present amendment to claim 1 is believed to obviate the claim rejection as to this claim.

Claim 1 was rejected under 35 USC 102(b) as being anticipated by ZABARA et al. 4,702,254. Claims 1-3 and 5 were rejected under 35 USC 102 (e) as being anticipated by KING et al. 2004/0210261. These rejections are respectfully traversed.

Claim 1 is amended to clarify that regulation of the at least one parameter is started in a state where the parameter is at a normal or unchanged level of the patient. Support for this feature can be found at least in paragraphs [0018] and [0036] of the application as filed.

Both Zabara and King relate to and execute methods in which respiratory parameters are diagnostic symptoms of the disease/disorder to be treated and vagus nerve stimulation (VNS) is based on the recognition of these symptoms. In Zabara and King VNS is under a feedback control where the symptoms of the disorder control the VNS. In these methods physiological

parameters, such as respiratory parameters are monitored on continuous basis. The diseases/disorders to be treated in both Zabara and King are characterized by seizures and/or attacks and the seizure and/or attack could be recognized for example by alterations in the numerical values of the respiratory parameters. The recognition of the seizure and/or attack is used to start the vagus nerve stimulation (VNS) and VNS is continued until the numerical values of the monitored parameters are normalized or got back to the acceptable range. In cases where the disease/disorder to be treated has no seizures and/or attacks, such as Parkinson disease, the exploitation of feedback control is not suggested (please see Zabara, from column 4 line 67 to column 5 line 10).

In contrast, in the present invention, the feedback control is not continuous. On the contrary it is used only during a short treatment period for finding the fixed settings for the stimulator/stimulus generator. In Zabara and King the feedback control is an automatic and built-in feature of the apparatus which is attached to the body. In the present invention, the feedback control is based on metering, which is made outside the body and the adjustment of the stimulator is based thereon, respectively. This is typically handwork of the nursing doctor.

Thus, as recited, the adjustment is based on monitoring of the respiratory parameters and the target is to find a stimulation level where the respiratory parameter shifts from its normal level.

Zabara and King on the other hand, trigger the stimulation based on the changes in the monitored parameters and control the stimulation towards the normal values based on the feedback of for example the respiratory parameters.

The Official Action offers column 5, lines 46 - 65 of Zabara where it is disclosed that "In a sense, the current parameters must be "tuned" to the specified nerve properties. It is for the foregoing reason that the pulse generator 10 is provided with means 12, 14 and 16 for varying the various current parameters of the pulse signal. The desired parameters are chosen by applying the electrodes (22 and 24) to the vagus nerve and varying
the current parameters until the desired clinical effect is produced. Since this "tuning" may have to be performed after the pulse generator is implanted, the present invention provides a means for varying the current parameters percutaneously. This is accomplished by a reed switch 30 associated with the implanted pulse generator 10 which is remotely controlled by electromagnet 32 and external programmer 34. The precise manner in which this is accomplished and the

circuitry associated therewith is well known to those skilled in the art as the same technique has been widely used in connection with the "tuning" of cardiac pacemakers."

The Official Action considers this to show that in Zabara physiological parameters, such as respiratory parameters are used to indicate that an adequate level of VNS stimulation is achieved.

Here the difference between Zabara and the presently recited invention is that in Zabara the regulation of VNS is continued until the desired clinical effect is produced. In Zabara the respiratory change is a symptom of the disease/disorder to be treated and a criterion which is used for controlling the VNS on a continuous basis (column 6, lines 52 to 62). Further, the VNS is controlled until the desired clinical effect is produced (column 5, lines 52 to 54). The respiratory change exists first and it is used for recognizing the need of VNS.

In the presently recited invention, respiratory change is not a symptom of the disease/disorder to be treated. The regulation of VNS is started in a state where the respiratory parameters of the patient are unchanged and/or normal. The regulation is used for finding the level

of stimulation which then produces the desired change in the respiratory parameter(s) from their normal or unchanged value(s).

The Official Action also offers column 6, lines 39-63 and Figure 3 of Zabara to show that Zabara also discloses a "sensor-feedback system" which includes a feedback loop for evaluating stimulation parameters' efficacy in abating a medical condition.

Here the difference between Zabara and the present invention is that in Zabara the regulation of VNS is continued during the seizure and/or attack, whereas in the present invention VNS is used with fixed settings (including timing of VNS) to prevent the occurrence of seizures/attacks.

With respect to King, the Official Action states that paragraph [0009] teaches that information relating to identified apneas or arousals can be used as feedback for adjusting characteristics of neurostimulation, e.g., amplitude, for subsequent delivery of neurostimulation in response to a detected apnea or associated arousal.

Here, it should be noted that the purpose of the feedback in King is to <u>restore</u> the normal respiration.

In contrast, in the presently recited invention, the respiration is normal or at the normal or un-changed level of the

patient in question in the starting point of the regulation. Stimulation is regulated until a desired change from the level of the starting point is achieved. Thereafter, stimulation is applied using fixed settings.

In Zabara and King the control of VNS (feedback) is based on the detection of a change in respiratory parameters which is due to the disorder/disease to be treated. The aim of this control is to restore the normal values of these respiratory parameters.

In the present invention, VNS is regulated until a change from the normal values of the respiratory parameters is achieved. This change is due to the direct effect of VNS on the control of respiration and is not dependent on the aimed effect of the treatment. Thereafter, stimulation is applied using fixed settings.

Based on at least this difference, the references are not anticipatory and rather, it could be concluded that Zabara and King teach away from the present invention.

Further, it is worth emphasizing that in the present invention vagus nerve stimulation (VNS) is applied in patients in whom a change in respiration is neither a symptom nor a cause of the clinical disorder, nor a diagnostic criterion of the

disorder. It should be understood that in the present invention VNS parameter values are pre-adjusted on the basis of VNS induced physiologically irrelevant respiratory changes, while the desired clinical effect - or the disorder that is to be cured - is not characterized by such respiratory changes.

The treatments of obesity or epilepsy give good examples. In the case of obesity, the desired clinical effect is weight loss. However, VNS intensity is not adjusted on the basis of measured changes in body weight, neither do respiratory changes provide any information on changes in body weight. Similarly, while VNS induced respiratory changes are used in the present invention to detect a sufficient level of stimulation that is low enough not to evoke any adverse effects, the respiratory changes are not symptoms of epilepsy that would be used to activate VNS.

A crucial difference should be very evident when VNS is used to treat e.g. apnea (as in King): An interruption of respiration - or the consequent increase in blood Pco2 - are characteristic symptoms of apnea and indicate the need of VNS. In other words, for example, in King et al, VNS is under a feedback control where the symptoms of the disorder control the VNS. In the present invention such a feedback control is nonexistent (adjustment is not based on any symptoms of the disorder but instead the VNS parameters are

pre-adjusted on the basis of VNS induced respiratory changes that are not related to the disorder).

The physiological changes, such as respiratory changes, that are monitored in Zabara and King have (patho)physiologic origin and they are symptoms of a disorder or a disease that needs to be treated. In the present invention, the respiratory changes are the consequence of VNS, thus having a totally different origin and additionally also a different purpose of use (i.e., the respiratory changes indicate that an adequate stimulation of VNS is achieved).

In summary the differences between the present invention and those described by King et al. and Zabara.

1. The present invention describes a method that allows easy and quick finding of proper stimulation parameter values that are thereafter used as fixed settings in the VNS device. In King and Zabara, physiological parameter values are being continuously monitored in the patient during everyday life and VNS parameter values are automatically altered to affect the detected (patho)physiological states. It should be noted that the only widely used application of VNS (treatment of epilepsy that is insensitive to antiepileptic drugs) relies on fixed VNS settings. Currently, finding clinically effective fixed VNS settings is a lengthy and expensive process including several

visits of the patient to the clinic. The present invention aids in finding adequate fixed VNS settings.

2. In the present invention, respiratory changes are minor artifacts induced by VNS and not related to the disorder that is to be cured by VNS. In King et al. and Zabara respiratory changes are symptoms of the (patho)physiological state that is to be cured by VNS. It should be noted that the origin of the respiratory changes is different.

3. In the present invention, respiratory changes are minor artifacts induced by VNS and used as indicators of the desired vagus nerve stimulation intensity. In King et al. and Zabara respiratory changes are symptoms of the (patho)physiological state and used as indicators telling that there is a need to stimulate vagus nerves. It should be noted that the aim of monitoring respiratory changes is different.

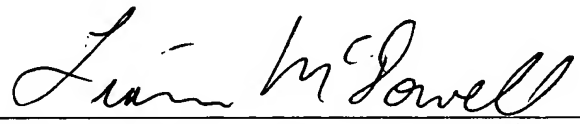
In view of the above, it is apparent that neither ZABARA nor KING use VNS in the manner recited and thus, are not anticipatory. Accordingly, reconsideration and withdrawal of the rejections are respectfully requested.

In view of the present amendment and the foregoing remarks, it is believed that the present application has been placed in condition for allowance. Reconsideration and allowance are respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



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